In the claims:

Please cancel, without prejudice, claims 106 and 110.

1. **(Previously presented)** An isolated protein comprising an N-terminal amino acid and a C-terminal amino acid, wherein the protein comprises an amino acid sequence selected from:

(a) an amino acid sequence with an N-terminal cysteine that is appended with at least one hydrophobic moiety;

(b) an amino acid sequence with an N-terminal amino acid that is not a cysteine appended with at least one hydrophobic moiety; and

(c) an amino acid sequence with at least one hydrophobic moiety substituted for the N-terminal amino acid,

wherein the protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched, and wherein said hydrophobic moiety enhances a biological activity of the protein.

2. **(Original)** The protein of claim 1, wherein the hydrophobic moiety is a peptide comprising at least one hydrophobic amino acid.

3. **(Original)** The protein of claim 1, wherein the hydrophobic moiety is a lipid.

~~4.~~ 5. **(Original)** The protein of claim 1, wherein the protein further comprises a hydrophobic moiety substituted for, or appended to, the C-terminal amino acid.

~~5.~~ 6. **(Original)** The protein of claim 1, wherein the protein is an extracellular signaling protein.

~~6.~~ 7. **(Original)** The protein of claim 1, wherein the N-terminal amino acid is a functional derivative of a cysteine.

8 (**Original**) The protein of claim 1, wherein the protein is modified at both the N-terminal amino acid and the C-terminal amino acid.

9 (**Previously presented**) The protein of claims 4 or 7, wherein the protein has a hydrophobic moiety substituted for, or appended to, at least one internal amino acid.

10 (**Original**) The protein of claim 1, wherein the protein has a hydrophobic moiety substituted for, or appended to, at least one amino acid intermediate to the N-terminal and C-terminal amino acids.

4 (**Original**) The protein of claim 3, wherein the lipid moiety is a fatty acid selected from saturated and unsaturated fatty acids having between 2 and 24 carbon atoms.

11-13. (**Cancelled**)

11 (**Original**) The protein of claim 1, further comprising a vesicle in contact with the hydrophobic moiety.

12 (**Previously presented**) The protein of claim 11, wherein the vesicle is selected from a cell membrane, a micelle, and a liposome.

16-27. (**Cancelled**)

14 (**Previously presented**) An isolated protein having a C-terminal amino acid and an N-terminal thioproline group, said group formed by reacting an aldehyde with an N-terminal cysteine of the protein, wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

15 (**Previously presented**) An isolated protein having a C-terminal amino acid and an N-terminal amide group, said group formed by reacting a fatty acid thioester with an N-terminal cysteine of the protein, wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

30. (**Previously presented**) An isolated protein having a C-terminal amino acid and an N-terminal maleimide group, said N-terminal maleimide group formed by reacting a maleimide group with the N-terminal cysteine of the protein, wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

31. (**Original**) The isolated protein of claims 28, 29 or 30, wherein the C-terminal amino acid of the protein is modified with a hydrophobic moiety.

32-39. (**Cancelled**)

40. (**Previously presented**) A method for modifying a physico-chemical property of a protein, comprising introducing at least one hydrophobic moiety to an N-terminal cysteine of the protein or to a functional equivalent of the N-terminal cysteine, wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

41. (**Original**) The method of claim 40, further comprising contacting the hydrophobic moiety with a vesicle.

42. (**Original**) The method of claim 40, wherein the hydrophobic moiety is either a lipid moiety selected from saturated and an unsaturated fatty acids having between 2 and 24 carbon atoms or is a hydrophobic protein.

43-45. (**Cancelled**)

46. (**Previously presented**) The method of claim 41, wherein the step of contacting comprises contacting with a vesicle selected from a cell membrane, liposome and micelle.

47. (**Cancelled**)

48. (**Original**) A modified protein, produced by the method of claim 40.

49. (**Cancelled**)

~~50~~ 26. **(Previously presented)** A method for modifying a protein having a biological activity and containing an N-terminal cysteine, comprising reacting the N-terminal cysteine with a fatty acid thioester to form an amide, wherein such modification enhances the protein's biological activity, wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

51-52. **(Cancelled)**

~~53~~ 27. **(Previously presented)** A method for modifying a protein having a biological activity and containing an N-terminal cysteine, comprising reacting the N-terminal cysteine with a maleimide group, wherein such modification enhances the protein's biological activity, wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

54-55. **(Cancelled)**

~~56~~ 28. **(Previously presented)** A method for modifying a protein that binds to an extracellular receptor, comprising appending a hydrophobic peptide to the protein, wherein the protein has a biological activity and the hydrophobic peptide enhances the biological activity, and wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

~~57~~ 29. **(Previously presented)** The method of claim ~~56~~ 28, wherein the hydrophobic peptide is appended to an amino acid of the protein selected from the N-terminal amino acid, the C-terminal amino acid, an amino acid intermediate between the N-terminal amino acid, and the C-terminal amino acid, and combinations of the foregoing.

58-62. **(Cancelled)**

~~63~~ 30. **(Original)** The method of claim ~~57~~ 29, wherein the step of appending comprises replacing at least the N- terminal amino acid of the protein with at least one hydrophobic amino acid.

64. (**Original**) The method of claim 63, wherein the at least one hydrophobic amino acid is a plurality of isoleucine residues.

65. (**Original**) The method of claim 63, further comprising chemically modifying at least one of the isoleucine residues.

66. (**Previously presented**) An isolated protein having a C-terminal amino acid and an N-terminal acetamide group, said group formed by reacting a substituted acetamide with an N-terminal cysteine of the protein, wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

67. (**Previously presented**) An isolated protein having a C-terminal amino acid and an N-terminal thiomorpholine group, said group formed by reacting a haloketone group with an N-terminal cysteine of the protein, wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

68. (**Previously presented**) A method for modifying a protein that binds to an extracellular domain of a cell membrane-associated receptor and contains an N-terminal cysteine, comprising reacting the N-terminal cysteine with a substituted acetamide group, wherein said protein has a biological activity, and the acetamide group enhances the biological activity of the protein, and wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

69-70. (**Cancelled**)

71. (**Previously presented**) A method for modifying a protein having a biological activity and containing an N-terminal cysteine, comprising reacting the N-terminal cysteine with a haloketone group, wherein such modification enhances the protein's biological activity, wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

72-86. (**Cancelled**)

87. **(Previously presented)** A method for modifying a protein that binds an extracellular domain of a cell membrane-associated receptor, comprising treating the protein with an active thioester under conditions sufficient to acylate the protein, wherein said protein has a biological activity, and acylation of the protein enhances the biological activity of the protein, and wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

88. **(Previously presented)** The method of claim 87, wherein the protein is acylated at an amino acid selected from the N-terminal amino acid, the C-terminal amino acid, an amino acid intermediate between the N-terminal amino acid and the C-terminal amino acid, and combinations of the foregoing.

89. **(Previously presented)** A method for modifying a protein that binds an extracellular domain of a cell membrane-associated receptor and contains an N-terminal cysteine, comprising reacting the N-terminal cysteine with a fatty acid active thioester to form an amide, wherein said protein has a biological activity, and the modification enhances the biological activity of the protein, and wherein said protein comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched.

90-92. **(Cancelled)**

93. **(Previously presented)** An isolated polypeptide ligand for a receptor, which receptor includes an extracellular domain and which receptor is membrane-associated, wherein the ligand comprises an amino acid sequence at least 80% identical to any of SEQ ID NOs: 1-4 and binds patched, and wherein said ligand is covalently attached to a hydrophobic moiety that enhances the biological activity of the ligand relative to the biological activity of the ligand in the absence of the hydrophobic moiety.

94. **(Previously presented)** The ligand of claim 93, wherein the hydrophobic moiety is a peptide comprising at least one hydrophobic amino acid.

95. (**Previously presented**) The ligand of claim 93, wherein the hydrophobic moiety is a lipid.

96. (**Previously presented**) The ligand of claim 93, wherein the protein further comprises a hydrophobic moiety substituted for, or appended to, the C-terminal amino acid.

97. (**Previously presented**) The ligand of claim 93, wherein the protein is an extracellular signaling protein.

98. (**Previously presented**) The ligand of claim 93, wherein the N-terminal amino acid is a functional derivative of a cysteine.

99. (**Previously presented**) The ligand of claim 93, wherein the ligand is modified at both the N-terminal amino acid and the C-terminal amino acid.

100. (**Previously presented**) The ligand of claim 96 or 99, wherein the ligand has a hydrophobic moiety substituted for, or appended to, at least one internal amino acid.

101. (**Previously presented**) The ligand of claim 93, wherein the ligand has a hydrophobic moiety substituted for, or appended to, at least one amino acid intermediate to the N-terminal and C-terminal amino acids.

102. (**Previously presented**) The ligand of claim 95, wherein the lipid moiety is a fatty acid selected from saturated and unsaturated fatty acids having between 2 and 24 carbon atoms.

103. (**Previously presented**) The ligand of claim 93, further comprising a vesicle in contact with the hydrophobic moiety.

104. (**Previously presented**) The ligand of claim 103, wherein the vesicle is selected from a cell membrane, a micelle, and a liposome.

105. (**Previously presented**) The protein of claim 1, wherein said protein binds patched and comprises an amino acid sequence at least 90% identical to any of SEQ ID NOs: 1-4.

106. (**Cancelled**)

107. (**Previously presented**) The protein of any of claims 28, 29 or 30, wherein said protein binds patched and comprises an amino acid sequence at least 90% identical to any of SEQ ID NOs: 1-4.

108. (**Previously presented**) The protein of claim 107, wherein said protein comprises an amino acid sequence identical to any of SEQ ID NOs: 1-4.

109. (**Previously presented**) The method of claim 40, wherein said protein binds patched and comprises an amino acid sequence at least 90% identical to any of SEQ ID NOs: 1-4.

110. (**Cancelled**)